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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,335	11/13/2003	Adolfo J. De Bold	14703-002001	1171

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
12/31/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/712,335	DE BOLD, ADOLFO J.	
	Examiner	Art Unit	
	VANESSA L. FORD	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 20-22* is/are pending in the application.

4a) Of the above claim(s) *22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This action is responsive to Applicant's amendment and response filed September 25, 2008. Claims 1-2 and 11-13 have been amended. Claims 14-19 and 23 have been cancelled.

Claim 22 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 27, 2006.

This application contains claim 22 drawn to an invention nonelected with traverse in the reply filed on September 27, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-13 and 20-21 are under examination.

Objections/Rejections Withdrawn

2. In view of Applicant's amendment and response the following objections/rejections have been withdrawn:

a) rejection of claims 1-21 under 35 U.S.C. 112 first paragraph, pages 3-8, paragraph 2.

b) rejection of claims 1-21 under 35 U.S.C. 112 first paragraph, pages 8-12, paragraph 3.

c) rejection of claim 11 under 35 U.S.C. 112 second paragraph, page 13, paragraph 4.

d) rejection of claim 11 under 35 U.S.C. 112 second paragraph, page 13, paragraph 5.

e) rejection of claims 1-3, 8-13 and 17-21 under 35 U.S.C. 102(b), pages 13-15, paragraph 6.

f) rejection of claims 1-3, 8-16 and 20-21 under 35 U.S.C. 102(b), pages 15-16, paragraph 7.

g) rejection of claims 1-3, 6-13, 17 and 19-20 under 35 U.S.C. 102(a), pages 16-17, paragraph 8.

h) rejection of claims 1-3, 6-13, 17 and 19-20 under 35 U.S.C. 102(b), pages 17-18, paragraph 9.

i) rejection of claims 1-4, 8-13 ad 17-21 under 35 U.S.C. 103(a), pages 18-21, paragraph 10.

j) rejection of claims 1-3, 5, 8-13 and 17-21 under 35 U.S.C. 103(a), pages 21-23, paragraph 11.

New Grounds of Rejection Necessitated by Applicant's Amendment

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-3, 6-13 and 20-21 are rejected under 35 U.S.C. 103(a) as patentable over Puyo et al *(Regulatory Peptides, Vol. 105, May 15, 2002, p. 139-143)* in view of Motwani et al *(Lancet, Vol,. 341, May 1, 1993, 1110-1113).*

Independent claim 1 is directed to a method of assisting in the diagnosis of cardiomyopathy, myocarditis or both, that arises as a result of an infection in a patient, comprising, obtaining a sample of a body fluid from the patient, and determining a level of a brain natriuretic peptide (BNP) or both BNP and atrial natriuretic peptide (ANF) within the sample of body fluid and comparing the level of BNP or both BNP and ANF to the level of BNP or both BNP and ANF from a control group, wherein an increase in the level of BNP or both BNP and ANF in the sample, compared to the level of BNP or both BNP and ANF in the control group, is an indicator of cardiomyopathy, mycarditis or both cardiomyopathy and mycarditis that arises as a result of an infection in a patient.

Puyo et al teach a method of determining atrial natriuretic peptide (ANF) levels in patients that are myocardial comprised (the Title and page 139). Puyo et al teach that

myocardial failure leads to increased ventricular production of ANF and BNP (page 139). Puyo et al teach that patients with chronic heart failure have high plasma concentration of both natriuretic peptides correlated with the extent of ventricular dysfunction (page 139). Puyo et al teach that Chagas' disease, one of the determinants of chronic heart failure and sudden cardiac death and is caused by a protozoan parasite *Trypanosoma cruzi* (page 139). Puyo et al teach that samples were taken from patients and plasma ANF was analyzed using radioimmunoassays (RIA) (page 140). Puyo et al teach that plasma ANF levels were elevated in patients with conduction defects and chronic heart failure of different origins (page 141). Puyo et al has demonstrated elevated plasma ANF levels in the acute but also in the chronic myocarditis induced by *T. cruzi* infection (page 142).

Puyo et al do not teach determining BNP levels in patients that are myocardial comprised.

Motwani et al teach a method of determining brain natriuretic peptide (BNP) levels in patients that have changes in ventricular function (page 1109). Motwani et al teach that plasma samples were taken from each patient in the study and assayed using radioimmunoassay (RIA) (page 1110). Motwani et al teach that anti-hBNP32 antibody was used in the study (page 1110). Motwani et al teach that in chronic heart failure, plasma BNP concentrations are substantially increased, the circulating concentration is proportional to the severity of heart failure (page 1111). Motwani et al teach that BNP is a unique marker of left-ventricular dysfunction at both early and late stages (pages 1111 and 1112).

It would have been *prima facie* obvious at the time the invention to modify the method of determining ANF levels in patients that are myocardial comprised as taught by Puyo et al to include the determination of BNP levels because Puyo et al teach that myocardial failure leads to increased ventricular production of ANF and BNP. It would be expected, absent evidence to the contrary, that determining ANF and BNP levels would be effective markers in determining patients that are myocardial comprised or have chronic heart failure.

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one composition and a person of ordinary skill would recognize that it would be used in similar compositions in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results". It is well known in the art that elevated levels of ANF are associated with patients that are myocardial comprised. See Puyo et al. It is well known in the art to detect ANF levels in myocardial comprised patients. See Puyo et al. It is known in the art to detect BNP levels in patients that have changes in ventricular function. See Motwani et al. Thus, it would be obvious to combine known methods to yield predictable results. The combination of references teach the claimed invention, absent convincing evidence to the contrary.

4. Claims 1-3, 6-13 and 20-21 are rejected under 35 U.S.C. 103(a) as patentable over Scaglione et al *(J Parasitol., Aug; 87(4):923-6)* in view of Motwani et al *(Lancet, Vol,. 341, May 1, 1993, 1110-1113).*

Independent claim 1 is directed to a method of assisting in the diagnosis of cardiomyopathy, myocarditis or both, that arises as a result of an infection in a patient, comprising, obtaining a sample of a body fluid from the patient, and determining a level of a brain natriuretic peptide (BNP) or both BNP and atrial natriuretic peptide (ANF) within the sample of body fluid and comparing the level of BNPor both BNP and ANF to the level of BNP or both BNP and ANF from a control group, wherein an increase in the level of BNP or both BNP and ANF in the sample, compared to the level of BNP or both BNP and ANF in the control group, is an indicator of cardiomyopathy, mycarditis or both cardiomyopathy and mycarditis that arises as a result of an infection in a patient.

Scaglione et al teach a method of determining atrial natriuretic peptide (ANF) levels in subjects have myocarditis produced by *Trypanosoma cruzi* infection (e.g. Chagas' disease)(see the Abstract). Scaglione et al teach that the highest plasma ANF levels were found in chronically infected could derived from the progressive failure of cardiac function (see the Abstract). Scaglione et al that plasma extraction and ANF radioimmunoassay (RIA) were performed on subjects (page 924). Scaglione et al teach that anti-rat ANF(99-126) were used in the assays (page 924). Scaglione et al teach that ANF and BNP are continuously released from the heart and they are found be elevated in different types of cardiovascular diseases (page 924).

Scaglione et al do not teach. determining BNP levels in patients that are myocardial comprised.

Motwani et al teach a method of determining brain natriuretic peptide (BNP) levels in patients that have changes in ventricular function (page 1109). Motwani et al teach that plasma samples were taken from each patient in the study and assayed using radioimmunoassay (RIA) (page 1110). Motwani et al teach that anti-hBNP32 antibody was used in the study (page 1110). Motwani et al teach that in chronic heart failure, plasma BNP concentrations are substantially increased, the circulating concentration is proportional to the severity of heart failure (page 1111). Motwani et al teach that BNP is a unique marker of left-ventricular dysfunction at both early and late stages (pages 1111 and 1112).

It would have been *prima facie* obvious at the time the invention to modify the method of determining ANF levels in patients that are myocardial comprised as taught by Scaglione et al to include the determination of BNP levels because Scaglione et al teach that ANF and BNP are continuously released from the heart and they are found be elevated in different types of cardiovascular diseases. It would be expected, absent evidence to the contrary, that determining ANF and BNP levels would be effective markers in determining patients that are myocardial comprised or have chronic heart failure.

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one composition and a person of ordinary skill would recognize that it would be used in similar compositions in the same

way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results". It is well known in the art that elevated levels of ANF are associated with chronic myocarditis . See Scaglione et al. .It is well known in the art to detect ANF levels in patients with chronic myocarditis. See Scaglione et al. It is known in the art to detect BNP levels in patients that have changes in ventricular function. See Motwani et al. Thus, it would be obvious to combine known methods to yield predictable results. The combination of references teach the claimed invention, absent convincing evidence to the contrary.

5. Claim 4 is rejected under 35 U.S.C. 103(a) as patentable over Scaglione et al and Motwani et al *(Lancet, Vol,. 341, May 1, 1993, 1110-1113)* as applied to claims 1-3, 6-13 and 20-21 and further in view of Marumo et al *(Clinical Chem, 36/9, p. 1650-1653, 1990)*.

Claim 4 is directed to the method of claim 1, wherein the body fluid comprise urine.

The teachings of Scaglione et al and Motwani et al have been described above.

Scaglione et al and Motwani et al do not teach the method of claim 1, wherein the body fluid comprises urine.

Marumo et al (1990) teach that atrial natriuretic peptide (ANP) is present in the urine (see the Title and page 1650).

It would have been *prima facie* obvious at the time the invention was made to substitute the body fluid sample, plasma for the body fluid sample, urine in a method of assisting in the diagnosis of cardiomyopathy, myocarditis or both, that arises as a result of an infection in a patient because Marumo et al (1990) teach that atrial natriuretic peptide (ANP) is present in the urine. It would be expected, absent evidence to the contrary, that a urine sample would be an appropriate sample to test for the presence of atrial natriuretic peptides.

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one composition and a person of ordinary skill would recognize that it would be used in similar compositions in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results". It is well known in the art that elevated levels of ANF are associated with patients with cardiovascular diseases. See Scaglione et al. It is well known in the art to that urine is a source of atrial natriuretic peptides. Marumo et al (1990). Thus, it would be obvious to use a known products from known sources in a method of diagnosis cardiomyopathy, myocarditis or both that is ready for improvement to yield predictable results.

6. Claim 5 is rejected under 35 U.S.C. 103(a) as patentable over Scaglione et al and Motwani et al *(Lancet, Vol,. 341, May 1, 1993, 1110-1113)* as applied to claims 1-3, 6-13 and 20-21 and further in view of Marumo et al *(Journal of Endocrinology, Vol. 119, Issue 1, p. 127-131, 1988) (Abstract only).*

Claim 5 is directed to the method of claim 1, wherein the body fluid comprise cerebrospinal fluid.

The teachings of Scaglione et al and Motwani et al have been described above.

Scaglione et al and Motwani et al do not teach the method of claim 1, wherein the body fluid comprises cerebrospinal fluid.

Marumo et al (1988) teach that atrial natriuretic peptide (ANP) is present in the cerebrospinal fluid (see the Abstract).

It would have been *prima facie* obvious at the time the invention was made to substitute the body fluid sample, plasma for the body fluid sample, cerebrospinal fluid in a method of assisting in the diagnosis of cardiomyopathy, myocarditis or both, that arises as a result of an infection in a patient because Marumo et al (1988) teach that atrial natriuretic peptide (ANP) is present in the cerebrospinal fluid. It would be expected, absent evidence to the contrary, that a cerebrospinal fluid sample would be an appropriate sample to test for the presence of atrial natriuretic peptides.

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one composition and a person of ordinary skill would recognize that it would be used in similar compositions in the same

way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results". It is well known in the art that elevated levels of ANF are associated with cardiovascular diseases . It is well known in the art to that cerebrospinal fluid is a source of atrial natriuretic peptides. See Marumo et al (1988). Thus, it would be obvious to use a known products from known sources in a method of diagnosis cardiomyopathy, myocarditis or both that is ready for improvement to yield predictable results.

Status of Claims

7. No claims allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Status of Claims

9. No claims allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Vanessa L. Ford/
Patent Examiner, Art Unit 1645
December 19, 2008

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645